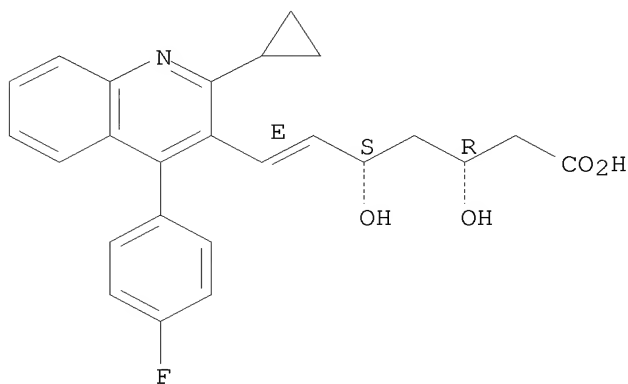


L1 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN  
RN 956116-90-8 REGISTRY  
ED Entered STN: 28 Nov 2007  
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, magnesium salt (2:1), (3R,5S,6E)- (CA INDEX NAME)  
OTHER NAMES:  
CN Pitavastatin magnesium  
FS STEREOSEARCH  
MF C25 H24 F N O4 . 1/2 Mg  
SR CA  
LC STN Files: CA, CAPLUS  
CRN (147511-69-1)

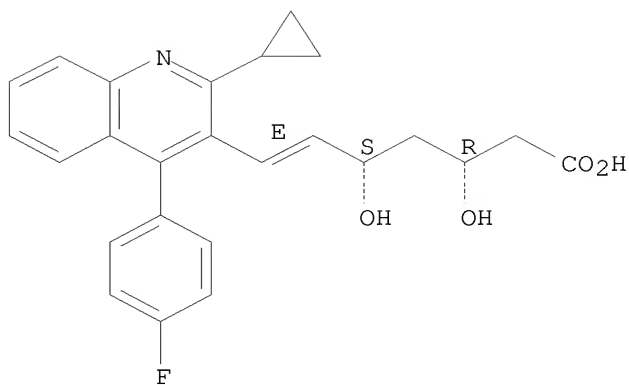
Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



2 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN  
RN 574705-92-3 REGISTRY  
ED Entered STN: 28 Aug 2003  
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, sodium salt (1:1), (3R,5S,6E)- (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)- (9CI)  
OTHER NAMES:  
CN Pitavastatin sodium  
FS STEREOSEARCH  
MF C25 H24 F N O4 . Na  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL  
CRN (147511-69-1)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.

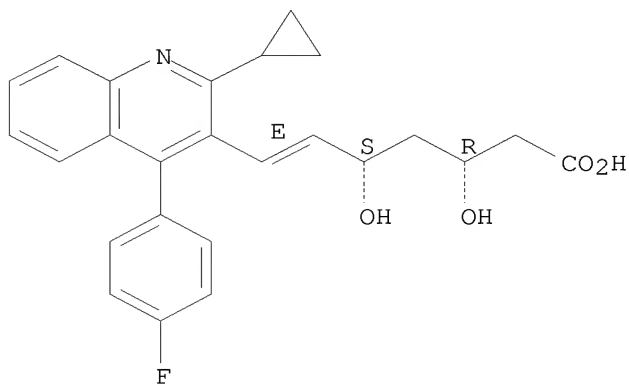


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5 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN  
 RN 192565-91-6 REGISTRY  
 ED Entered STN: 14 Aug 1997  
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, potassium salt (1:1), (3R,5S,6E)- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monopotassium salt, [S-[R\*,S\*-(E)]]- (9CI)  
 OTHER NAMES:  
 CN Pitavastatin potassium  
 FS STEREOSEARCH  
 MF C25 H24 F N O4 . K  
 SR CA  
 LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE  
 CRN (147511-69-1)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



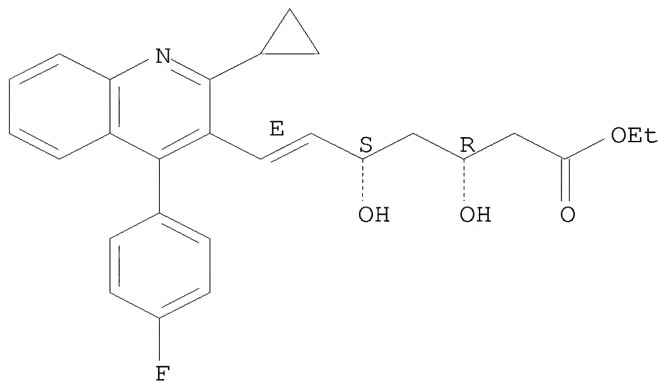
● K

3 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN  
RN 167073-19-0 REGISTRY  
ED Entered STN: 31 Aug 1995  
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, [S-[R\*,S\*-(E)]]-  
OTHER NAMES:  
CN (3R,5S,6E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-6-heptenoic acid ethyl ester  
CN 3R,5S-DOLE  
CN Ethyl (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate  
CN Pitavastatin ethyl ester  
CN [3R,5S(E)]-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate  
FS STEREOSEARCH  
MF C27 H28 F N O4  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, PS, USPAT2, USPATFULL

Absolute stereochemistry.  
Double bond geometry as shown.



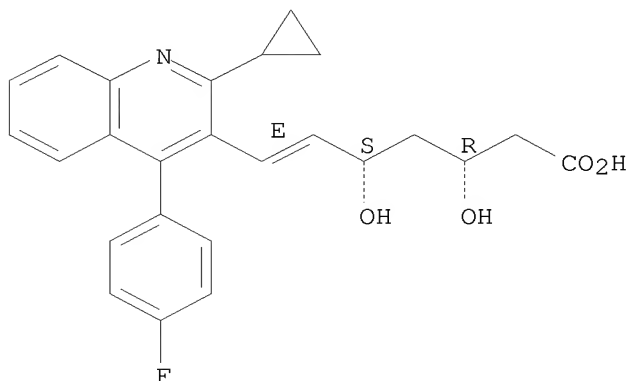
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

15 REFERENCES IN FILE CA (1907 TO DATE)  
15 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN  
RN 147526-32-7 REGISTRY  
ED Entered STN: 13 May 1993  
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), [S-[R\*,S\*-(E)]]-  
OTHER NAMES:  
CN (E)-(3R,5S)-7-[2-Cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid hemicalcium salt  
CN Flovas  
CN Livalo  
CN NK 104

CN NK 104 (acid)  
 CN Pitava  
 CN Pitava 1  
 CN Pitavastatin calcium  
 CN Pitavastatin hemicalcium  
 FS STEREOSEARCH  
 MF C25 H24 F N O4 . 1/2 Ca  
 SR CA  
 LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA,  
 CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, EMBASE, IMSPATENTS,  
 IMSRESEARCH, IPA, MEDLINE, MRCK\*, PHAR, PROMT, PROUSDDR, PS, RTECS\*,  
 SCISEARCH, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 CRN (147511-69-1)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

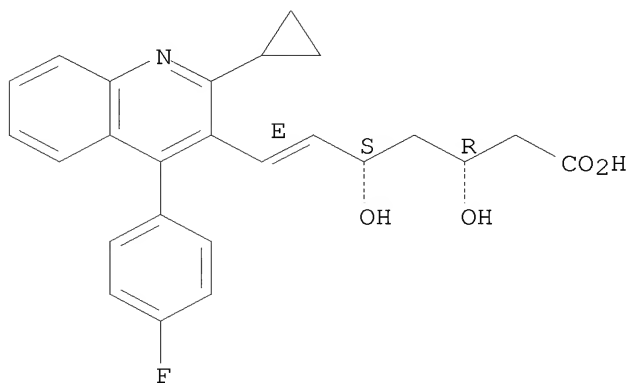
113 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 114 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN  
 RN 147511-69-1 REGISTRY  
 ED Entered STN: 13 May 1993  
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, [S-[R\*,S\*-(E)]]-  
 OTHER NAMES:  
 CN (+)-(3R,5S,6E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-3-quinolyl]-3,5-dihydroxy-6-heptenoic acid  
 CN (3R,5S,6E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid  
 CN NK 104  
 CN Pitavastatin  
 FS STEREOSEARCH  
 MF C25 H24 F N O4  
 CI COM  
 SR CA  
 LC STN Files: ADISINSIGHT, AGRICOLA, BIOSIS, CA, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA,

MRCK\*, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2,  
USPATFULL

(\*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

547 REFERENCES IN FILE CA (1907 TO DATE)  
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
552 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
20.07	20.28

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 11:15:00 ON 01 APR 2008

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 1 Apr 2008 VOL 148 ISS 14

FILE LAST UPDATED: 31 Mar 2008 (20080331/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s 147511-69-1/rn <> or pitavastatin?

MISSING TERM '-69-1/RN <> OR'

The search profile that was entered contains a logical operator followed immediately by another operator.

=> s l1 <> or pitavastatin?

SmartSELECT INITIATED  
New TRANSFER and ANALYZE Commands Now Available  
See HELP TRANSFER and HELP ANALYZE for Details

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.48	20.76

FILE 'REGISTRY' ENTERED AT 11:15:46 ON 01 APR 2008  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2008 American Chemical Society (ACS)

SET SMARTSELECT ON  
SET COMMAND COMPLETED

SEL L1 1-  
L2 SEL L1 1- CHEM : 33 TERMS

SET SMARTSELECT OFF  
SET COMMAND COMPLETED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.11	32.87

FILE 'CAPLUS' ENTERED AT 11:15:47 ON 01 APR 2008  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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S L2 OR PITAVASTATIN?

L4 515 PITAVASTATIN?  
725 L3 OR PITAVASTATIN?

=> s l4 and pd <-2002  
21909301 PD <-2002  
(PD<20020000)  
L5 102 L4 AND PD <-2002

=> s l4 and pd <=2002  
22882229 PD <=2002  
(PD<=20029999)  
L6 168 L4 AND PD <=2002

=> delete l5  
DELETE L5? (Y)/N:y  
'L5' DELETED

=> s l6 and (antithromb? or thrombus OR "Anticoagulants" OR "Anticoagulants" OR  
"Thrombus" and "Blood clot" OR "Thrombus and(or) Blood clot" OR "Thrombus" OR  
"Blood coagulation" OR "Platelet (blood)" OR "Platelet aggregation" or  
thrombosis or plasminogen or plasmin)  
24886 ANTITHROMB?  
9637 THROMBUS  
2 THROMBUSES  
2746 THROMBI  
16 THROMBIS  
11113 THROMBUS

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        (THROMBUS OR THROMBUSES OR THROMBI OR THROMBIS)
25082 "ANTICOAGULANTS"
25082 "ANTICOAGULANTS"
9637 "THROMBUS"
2 "THROMBUSES"
2746 "THROMBI"
16 "THROMBIS"
11113 "THROMBUS"
        ("THROMBUS" OR "THROMBUSES" OR "THROMBI" OR "THROMBIS")
1371783 "BLOOD"
1293 "BLOODS"
1371932 "BLOOD"
        ("BLOOD" OR "BLOODS")
9827 "CLOT"
3600 "CLOTS"
11823 "CLOT"
        ("CLOT" OR "CLOTS")
3669 "BLOOD CLOT"
        ("BLOOD" (W) "CLOT")
9637 "THROMBUS"
2 "THROMBUSES"
2746 "THROMBI"
16 "THROMBIS"
11113 "THROMBUS"
        ("THROMBUS" OR "THROMBUSES" OR "THROMBI" OR "THROMBIS")
0 "AND"
293 "ANDS"
293 "AND"
        ("AND" OR "ANDS")
0 "OR"
2016 "ORS"
2016 "OR"
        ("OR" OR "ORS")
1371783 "BLOOD"
1293 "BLOODS"
1371932 "BLOOD"
        ("BLOOD" OR "BLOODS")
9827 "CLOT"
3600 "CLOTS"
11823 "CLOT"
        ("CLOT" OR "CLOTS")
0 "THROMBUS AND (OR) BLOOD CLOT"
        ("THROMBUS" (W) "AND" (W) "OR" (W) "BLOOD" (W) "CLOT")
9637 "THROMBUS"
2 "THROMBUSES"
2746 "THROMBI"
16 "THROMBIS"
11113 "THROMBUS"
        ("THROMBUS" OR "THROMBUSES" OR "THROMBI" OR "THROMBIS")
1371783 "BLOOD"
1293 "BLOODS"
1371932 "BLOOD"
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115789 "COAGULATION"
218 "COAGULATIONS"
115860 "COAGULATION"
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50273 "BLOOD COAGULATION"
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118884 "PLATELET"
57892 "PLATELETS"
135820 "PLATELET"
        ("PLATELET" OR "PLATELETS")
1371783 "BLOOD"
1293 "BLOODS"
1371932 "BLOOD"

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                ("BLOOD" OR "BLOODS")
22349 "PLATELET (BLOOD)"
                ("PLATELET" (W) "BLOOD")
118884 "PLATELET"
57892 "PLATELETS"
135820 "PLATELET"
                ("PLATELET" OR "PLATELETS")
118485 "AGGREGATION"
2418 "AGGREGATIONS"
120065 "AGGREGATION"
                ("AGGREGATION" OR "AGGREGATIONS")
30869 "PLATELET AGGREGATION"
                ("PLATELET" (W) "AGGREGATION")
27392 THROMBOSIS
1 THROMBOSISES
27393 THROMBOSIS
                (THROMBOSIS OR THROMBOSISES)
31041 PLASMINOGEN
180 PLASMINOGENS
31051 PLASMINOGEN
                (PLASMINOGEN OR PLASMINOGENS)
12320 PLASMIN
67 PLASMINS
12330 PLASMIN
                (PLASMIN OR PLASMINS)
L7      15 L6 AND (ANTITHROMB? OR THROMBUS OR "ANTICOAGULANTS" OR "ANTICOA
                GULANTS" OR "THROMBUS" AND "BLOOD CLOT" OR "THROMBUS AND(OR)
                BLOOD CLOT" OR "THROMBUS" OR "BLOOD COAGULATION" OR "PLATELET
                (BLOOD)" OR "PLATELET AGGREGATION" OR THROMBOSIS OR PLASMINOGEN
                OR PLASMIN)

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=> focus
PROCESSING COMPLETED FOR L7
L8      15 FOCUS L7 1-

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L8      ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2008 ACS on STN

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ACCESSION NUMBER:      2001:171636  CAPLUS

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DOCUMENT NUMBER:      135:147210

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TITLE:      General pharmacological study of an
                anti-hyperlipidemic agent, NK-104

```

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AUTHOR(S):      Yoshinaka, Yasunobu; Suzuki, Hideo; Tamaki, Taro;
                Sato, Fumiyasu; Wada, Yasushi

```

```

CORPORATE SOURCE:      Tokyo Res. Lab. Pharmaceutical Div., Kowa Company
                Ltd., Japan

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SOURCE:      Japanese Pharmacology & Therapeutics (2001),
                29(1), 59-72
                CODEN: JPTABU

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PUBLISHER:      Raifu Saiensu Shuppan K.K.

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DOCUMENT TYPE:      Journal

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LANGUAGE:      Japanese

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AB      The general pharmacol. of NK-104, a new competitive
                inhibitor of 3-hydroxy-3-ethyl-glutaryl CoA (HMG-CoA) reductase, was
                studied in exptl. animals. NK-104 (3-30 mg/kg, p.o.)
                had no significant effects on the gross behavior, spontaneous locomotor
                activity, hexobarbital-induced anesthesia, electroshock seizure,
                pentylenetetrazol-induced convulsions in mice and body temperature in rats,

```

```

and

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                it did not influence on muscle relaxation in mice. In the analgesic
                measurement, NK-104 (10-30 mg/kg) inhibited the acetic
                acid-induced writhing in mice, but had no effects on the tail pinch
                response of Haffner method at the same dose in mice. With respect to
                smooth muscle response, NK-104 significantly inhibited
                the acetylcholine-, histamine- and barium chloride-induced contractions in
                isolated guinea pig ileum at a concentration of 10-4 M. Concerning the

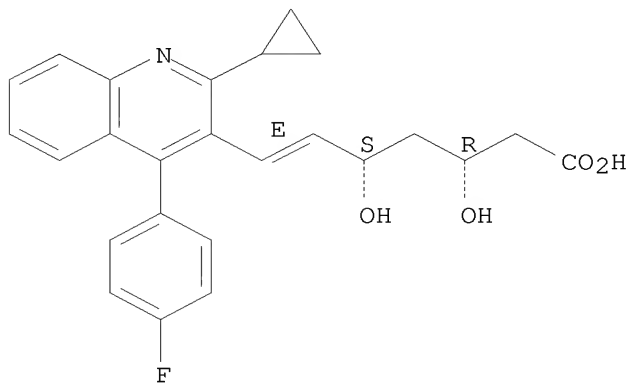
```

respiratory and cardiovascular system, NK-104 (0.3-3 mg/kg, i.v.) had no effect on respiration, blood pressure, heart rate, ECG, femoral blood flow, acetylcholine-induced depressor response and norepinephrine induced pressor response in anesthetized dogs. In the digestive system, NK-104 had no effect on the intestinal propulsion in mice, on gastric secretion and bile secretion in rats, and it did not induce gastric lesions in rats. Repeated administration of NK-104 (3 mg/kg/day, p.o. for 15 days) to guinea pigs caused no effect on the lithogenic index of bile irres. of the reduction of the plasma cholesterol level. With respect to the

influence of NK-104 on urinary system, NK-104 reduced the Na<sup>+</sup> and Cl<sup>-</sup> excretion at doses of 10 and 30 mg/kg and reduced the urinary volume at a dose of 30 mg/kg. In addition, NK-104 did not affect the blood coagulation and platelet aggregation at the concentration of 10<sup>-7</sup>-10<sup>-4</sup> M. From above results the changes observed in those parameters were slight or mild and each ineffective dose or concentration was higher than the min. hypolipidemic dose (0.1 mg/kg, p.o.) or Ki value (1.7 nM). Therefore, it seemed that NK-104 would be free from any serious acute adverse effects clin.

IT 147526-32-7, NK-104  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (general pharmacol. study of anti-hyperlipidemic agent NK-104)  
 RN 147526-32-7 CAPLUS  
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



● 1/2 Ca

L8 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2002:392219 CAPLUS  
 DOCUMENT NUMBER: 136:406945  
 TITLE: Methods for in vivo drug delivery based on monitoring blood flow parameters  
 INVENTOR(S): Kensey, Kenneth R.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 727,950.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent

LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 8  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020061835	A1	20020523	US 2001-828761	20010409 <--
US 6019735	A	20000201	US 1997-919906	19970828 <--
CA 2301161	A1	19990304	CA 1998-2301161	19980826 <--
WO 9910724	A2	19990304	WO 1998-US17657	19980826 <--
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RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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US 6322524	B1	20011127	US 1999-439795	19991112 <--
US 6322525	B1	20011127	US 2000-501856	20000210 <--
NO 2000000944	A	20000225	NO 2000-944	20000225 <--
MX 200002073	A	20010821	MX 2000-2073	20000228 <--
US 6428488	B1	20020806	US 2000-615340	20000712 <--
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WO 2002043806	A2	20020606	WO 2001-US44352	20011127 <--
WO 2002043806	A3	20030327		
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AU 2002026986	A	20020611	AU 2002-26986	20011127 <--
US 20020088953	A1	20020711	US 2001-33841	20011227 <--
US 6624435	B2	20030923		
WO 2002079778	A2	20021010	WO 2002-US3984	20020207 <--
WO 2002079778	A3	20030710		
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US 20020184941	A1	20021212	US 2002-156165	20020528 <--
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PRIORITY APPLN. INFO.:

US 1997-919906	A2 19970828
US 1999-439795	A2 19991112
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US 1997-966076	A 19971107
WO 1998-US17657	W 19980826
US 2000-615340	A3 20000712
US 2000-228612P	P 20000828
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US 2001-819924	A 20010328
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US 2001-839785	A 20010420
US 2001-841389	A 20010424
US 2001-897164	A3 20010702
WO 2001-US44352	W 20011127

AB Various methods are provided for determining and utilizing the viscosity of the

circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IT 147511-69-1, Pitavastatin

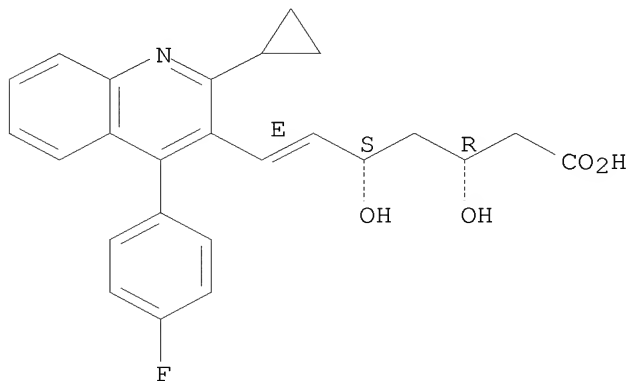
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods for in vivo drug delivery based on monitoring blood flow parameters)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoliny]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



L8 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:185688 CAPLUS

DOCUMENT NUMBER: 136:252567

TITLE: Methods for drug administration and distribution based on monitoring blood viscosity and other parameters for diagnostics and treatment

INVENTOR(S): Kensey, Kenneth

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S.  
 Ser. No. 819,924.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 8  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9910724	A2	19990304	WO 1998-US17657	19980826 <--
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US 6322524	B1	20011127	US 1999-439795	19991112 <--
US 6322525	B1	20011127	US 2000-501856	20000210 <--
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US 6428488	B1	20020806	US 2000-615340	20000712 <--
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US 20020184941	A1	20021212	US 2002-156165	20020528 <--
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US 2001-828761	A 20010409
US 2001-839785	A 20010420
US 2001-841389	A 20010424
US 2001-897164	A3 20010702

AB Various methods are provided for determining and utilizing the viscosity of the

circulating blood of a living being, i.e., a human, over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream. For example, when blood viscosity is a blood flow parameter monitored, an agent is selected from i.v. diluents, red blood cell deformability agents, antiurea agents, oral contraceptives, antidiabetic agents, antiarrhythmics, antihypertensives, antihyperlipidemics, antiplatelet agents, appetite suppressants, antiobesity agents, blood modifiers, smoking deterrent agents, and nutritional supplements.

IT 147511-69-1, Pitavastatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(apparatus and methods for monitoring blood viscosity and other

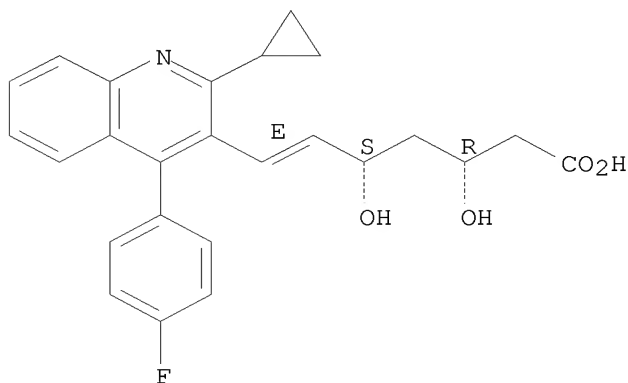
parameters

in drug delivery for diagnostics and treatment)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



L8 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:319495 CAPLUS

DOCUMENT NUMBER: 138:343864

TITLE: In vivo delivery methods and compositions

INVENTOR(S): Kensey, Kenneth

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S. Ser. No. 819,924.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030078517	A1	20030424	US 2001-839785	20010420
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US 6322524	B1	20011127	US 1999-439795	19991112 <--
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NO 2000000944	A	20000225	NO 2000-944	20000225 <--
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US 6428488	B1	20020806	US 2000-615340	20000712 <--
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US 20020184941	A1	20021212	US 2002-156165	20020528 <--
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US	2000-727950	B2	20001201
US	2001-819924	A2	20010328
US	1997-966076	A	19971107
WO	1998-US17657	W	19980826
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WO	2001-US44352	W	20011127

AB Various methods are provided for determining and utilizing the viscosity of the

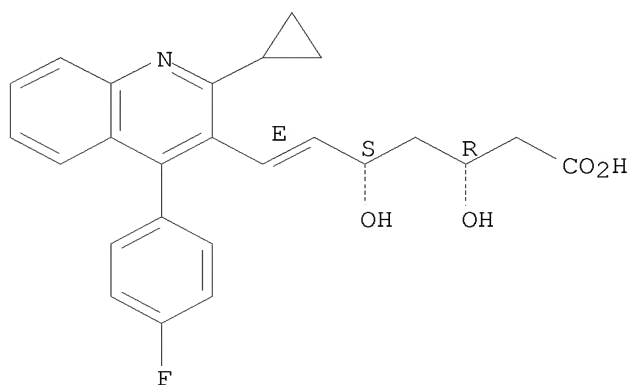
circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least 1 drug. Agents effective to regulate at least 1 of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IT 147511-69-1, Pitavastatin  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (in vivo delivery methods and compns.)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



L8 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:428760 CAPLUS

DOCUMENT NUMBER: 137:24314

TITLE: Methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment

INVENTOR(S): Kensey, Kenneth; Hokanson, Charles

PATENT ASSIGNEE(S): Visco Technologies, Inc., USA; Rheologics, Inc.

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

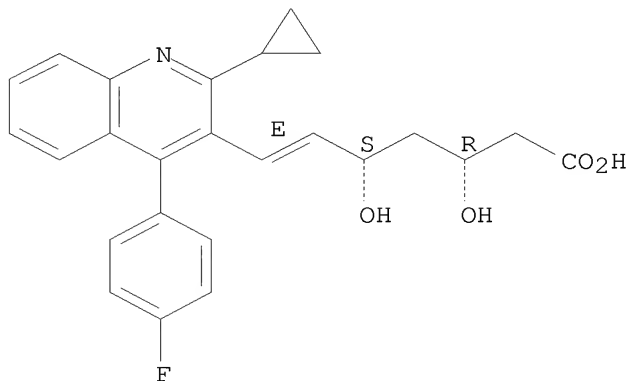
DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 8  
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			US 1999-439795	A2 19991112
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			WO 2001-US44352	W 20011127
AB	Various methods are provided for determining and utilizing the viscosity of the			
the	circulating blood of a living being over a range of shear rates for			
	diagnostics and treatment, such as detecting/reducing blood viscosity,			
	work of the heart, contractility of the heart, for detecting/reducing the			
	surface tension of the blood, for detecting plasma viscosity, for			
	explaining/countering endothelial cell dysfunction, for providing high and			
	low blood vessel wall shear stress data, red blood cell deformability			
	data, lubricity of blood, and for treating different ailments such as			
	peripheral arterial disease in combination with administering to a living			
	being at least one pharmaceutically acceptable agent. Agents			
	pharmaceutically effective to regulate at least one of the aforementioned			
	blood parameters are used to adjust distribution of a substance through			
	the bloodstream.			
IT	147511-69-1, Pitavastatin			
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(methods and apparatus for determining and utilizing the viscosity of			
	circulating			

blood over a range of shear rates for diagnostics and treatment)  
 RN 147511-69-1 CAPLUS  
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.

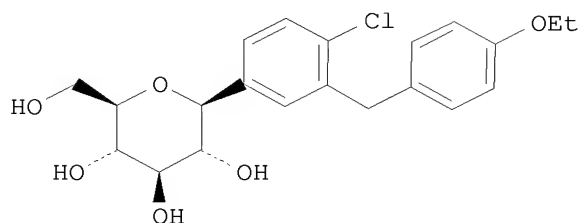


L8 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2002:736927 CAPLUS  
 DOCUMENT NUMBER: 137:247879  
 TITLE: Preparation of antidiabetic agents C-aryl glucoside as human SGLT2 inhibitors  
 INVENTOR(S): Ellsworth, Bruce; Washburn, William N.; Sher, Philip M.; Wu, Gang; Meng, Wei  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 6,414,126.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6515117	B2	20030204		
CN 1896088	A	20070117	CN 2006-10093189	20001002
US 6414126	B1	20020702	US 2000-679027	20001004 <--
ZA 2002002604	A	20030703	ZA 2002-2604	20020403
CA 2486539	A1	20031204	CA 2003-2486539	20030515
WO 2003099836	A1	20031204	WO 2003-US15591	20030515
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003237886	A1	20031212	AU 2003-237886	20030515
EP 1506211	A1	20050216	EP 2003-736643	20030515
EP 1506211	B1	20070207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011323	A	20050315	BR 2003-11323	20030515

CN 1653075	A	20050810	CN 2003-811353	20030515
JP 2005531588	T	20051020	JP 2004-507493	20030515
AT 353334	T	20070215	AT 2003-736643	20030515
NZ 536605	A	20070531	NZ 2003-536605	20030515
ES 2280759	T3	20070916	ES 2003-736643	20030515
CN 101092409	A	20071226	CN 2007-10108986	20030515
NO 2004004915	A	20041216	NO 2004-4915	20041111
MX 2004PA11371	A	20050214	MX 2004-PA11371	20041116
IN 2004DN03573	A	20050401	IN 2004-DN3573	20041116
ZA 2004009295	A	20060222	ZA 2004-9295	20041118
HK 1068214	A1	20070824	HK 2005-101975	20050308
PRIORITY APPLN. INFO.:			US 1999-158773P	P 19991012
			US 2000-194615P	P 20000405
			US 2000-679027	A2 20001004
			CN 2000-816741	A3 20001002
			US 2002-151436	A 20020520
			CN 2003-811353	A3 20030515
			WO 2003-US15591	W 20030515

GI



I

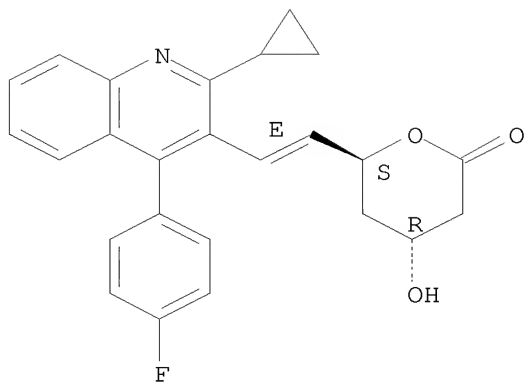
AB A SGLT2-inhibiting compound is provided having the formula I method is also provided for treating diabetes and related diseases employing a SGLT2-inhibiting amount of the above compound alone or in combination with another antidiabetic agent or other therapeutic agent (no data). 1A pharmaceutical combination comprising a SGLT2 inhibitor compound and an antidiabetic agent other than a SGLT2 inhibitor, for treating the complications of diabetes, an antiobesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent, and/or a lipid-lowering agent (no data). A method for treating or delaying the progression or onset of diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension, or for increasing high-d. lipoprotein levels, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compd (no data).

IT 141750-63-2, Nisvastatin  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of antidiabetic agents C-aryl glucosides as human SGLT2 inhibitors)

RN 141750-63-2 CAPLUS

CN 2H-Pyran-2-one, 6-[(1E)-2-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]ethenyl]tetrahydro-4-hydroxy-, (4R,6S)- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L8 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:392237 CAPLUS

DOCUMENT NUMBER: 136:401651

TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors

INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing  
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.

CODEN: USXXCO

DOCUMENT TYPE: Patent

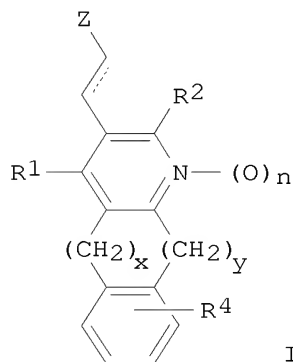
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

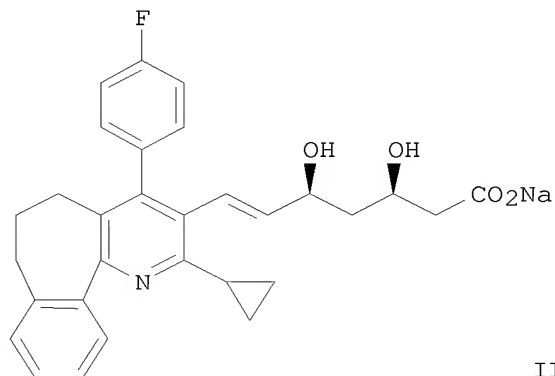
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020061901	A1	20020523	US 2001-8154	20011204 <--
US 6620821	B2	20030916		
US 20020028826	A1	20020307	US 2001-875218	20010606 <--
US 20040024216	A1	20040205	US 2003-602753	20030624
PRIORITY APPLN. INFO.:			US 2000-211594P	P 20000615
			US 2001-875218	A2 20010606
			US 2001-8154	A3 20011204

OTHER SOURCE(S): MARPAT 136:401651  
GI



I



II

AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z =

CH(OH)CH<sub>2</sub>CR<sup>7</sup>(OH)CH<sub>2</sub>CO<sub>2</sub>R<sup>3</sup> or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH<sub>2</sub>)<sub>x</sub> and/or (CH<sub>2</sub>)<sub>y</sub> together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R<sup>1</sup>, R<sup>2</sup> = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R<sup>3</sup> = H or lower alkyl; R<sup>4</sup> = H, halo, CF<sub>3</sub>, OH, alkyl, alkoxy, CO<sub>2</sub>H, (un)substituted NH<sub>2</sub>, cyano, (un)substituted CONH<sub>2</sub>, etc.; R<sup>7</sup> = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Preps. of several compds. are described. For instance, a multistep synthesis of fused pyridine derivative II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.

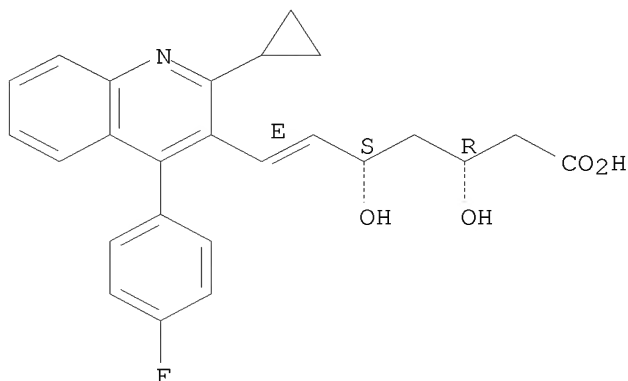
II 147511-69-1, Pitavastatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(therapeutic compns. containing; preparation of fused pyridine derivs. as HMG-CoA reductase inhibitors)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoliny]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



L8 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:777650 CAPLUS

DOCUMENT NUMBER: 137:299910

TITLE: Therapeutic combinations containing COX-2 inhibitors for cardiovascular and inflammatory diseases treatment  
INVENTOR(S): Seibert, Karen; Keller, Bradley T.; Isakson, Peter C.; Krul, Elaine S.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 316 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002078626	A2	20021010	WO 2002-US9346	20020328 <--

WO 2002078626 A3 20040429

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2442328 A1 20021010 CA 2002-2442328 20020328 <--  
AU 2002255929 A1 20021015 AU 2002-255929 20020328 <--  
US 20030199482 A1 20031023 US 2002-107809 20020328  
EP 1435956 A2 20040714 EP 2002-725362 20020328

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

CN 1527709 A 20040908 CN 2002-810210 20020328  
JP 2005507854 T 20050324 JP 2002-576894 20020328  
MX 2003PA08835 A 20041206 MX 2003-PA8835 20030929  
US 20040186154 A1 20040923 US 2004-473045 20040506

PRIORITY APPLN. INFO.: US 2001-279239P P 20010328  
WO 2002-US9346 W 20020328

AB The present invention provides therapeutic combinations and methods for treating or preventing a hypercholesterolemia-related or an inflammation-related condition in a subject in need of such treatment or prevention. One therapeutic combination comprises an ASBT inhibitor combined with COX-2 inhibitor. A further therapeutic combination comprises an ASBT inhibitor, a COX-2 inhibitor and an HMG Co-A reductase inhibitor. Another therapeutic combination comprises a chromene COX-2 inhibitor and an HMG Co-A reductase inhibitor. Thus, a tablet composition contained benzothiepine 5, celecoxib 20, lactose 54, microcryst. cellulose 15, HPMC 3, Croscarmellose sodium 2, and Mg stearate 1 mg/tablet.

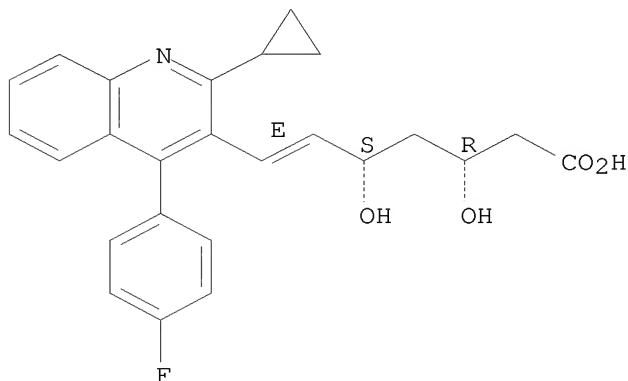
IT 147511-69-1, Itavastatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(therapeutic combinations containing COX-2 inhibitors for cardiovascular and inflammatory diseases treatment)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoliny]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



L8 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:283949 CAPLUS

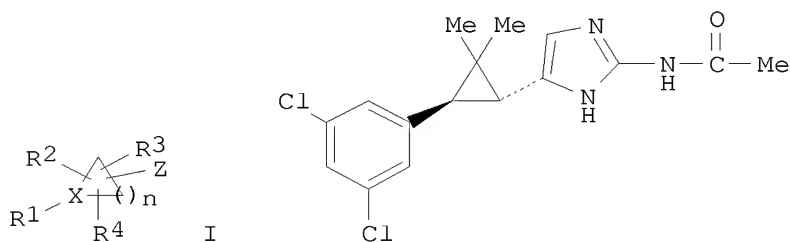
DOCUMENT NUMBER: 134:311218

TITLE: Synthesis and use of heterocyclic sodium/proton  
exchange inhibitors

INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 221 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027107	A2	20010419	WO 2000-US27461	20001002 <--
WO 2001027107	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6887870	B1	20050503	US 2000-669298	20000925
CA 2388813	A1	20010419	CA 2000-2388813	20001002 <--
EP 1224183	A2	20020724	EP 2000-968723	20001002 <--
EP 1224183	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000014725	A	20030617	BR 2000-14725	20001002
HU 2003000195	A2	20030728	HU 2003-195	20001002
HU 2003000195	A3	20030929		
JP 2003527331	T	20030916	JP 2001-530325	20001002
NZ 517668	A	20040924	NZ 2000-517668	20001002
AT 314364	T	20060115	AT 2000-968723	20001002
ES 2254236	T3	20060616	ES 2000-968723	20001002
IN 2002MN00354	A	20050318	IN 2002-MN354	20020322
ZA 2002002479	A	20040727	ZA 2002-2479	20020327
MX 2002PA03626	A	20030922	MX 2002-PA3626	20020410
NO 2002001717	A	20020610	NO 2002-1717	20020411 <--
US 20050137216	A1	20050623	US 2005-46993	20050131
US 7326705	B2	20080205		
PRIORITY APPLN. INFO.:			US 1999-158755P	P 19991012
			US 2000-669298	A3 20000925
			WO 2000-US27461	W 20001002

OTHER SOURCE(S): MARPAT 134:311218  
 GI



AB Compds. of formula I [wherein; n is 1-5; X is N or CR5, where R5 is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R1 is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R2, R3 and R4 are any of the groups set out for R1 and optionally

substituted with 1 to 5 substituents which may be the same or different and when X is N, R<sub>1</sub> is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding  $\alpha$ -chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents,  $\beta$ -adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT 147511-69-1, Itavastatin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

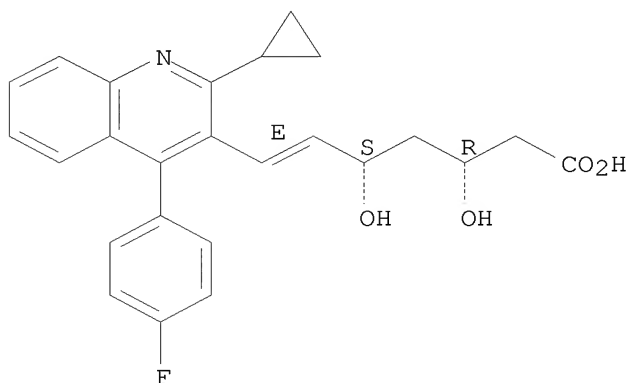
(pharmaceuticals containing; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



L8 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:744783 CAPLUS

DOCUMENT NUMBER: 138:297319

TITLE: The effect of statins on mRNA levels of genes related to inflammation, coagulation, and vascular constriction in HUVEC

AUTHOR(S): Morikawa, Shigeru; Takabe, Wakako; Mataka, Chikage; Kanke, Toru; Itoh, Takahiro; Wada, Youichiro; Izumi, Akashi; Saito, Yasushi; Hamakubo, Takao; Kodama, Tatsuhiko

CORPORATE SOURCE: Departments of Molecular Biology and Medicine, Research Center for Advanced Science and Technology, University of Tokyo, Tokyo, Japan

SOURCE: Journal of Atherosclerosis and Thrombosis (2002), 9(4), 178-183

CODEN: JATHEH; ISSN: 1340-3478

PUBLISHER: Japan Atherosclerosis Society

DOCUMENT TYPE: Journal

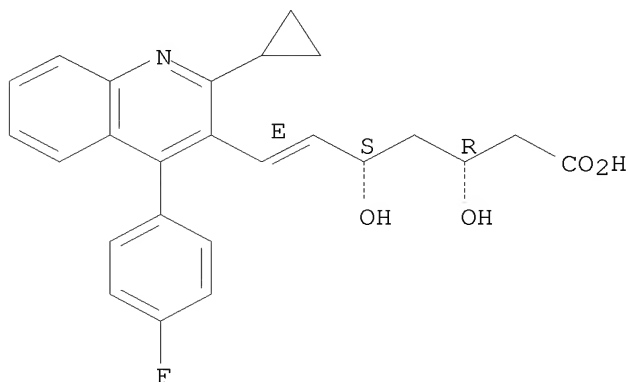
LANGUAGE: English

AB Large-scale clin. trials have demonstrated significant redns. in cardiovascular events following statin therapy. The observed benefit of statin therapy, however, may be greater in these trials than is to be

expected from lowering lipid levels alone. In order to clarify the mechanism by which statins prevent cardiovascular events in vascular wall cells, we investigated the changes in gene expression profiles after incubation with atorvastatin or pitavastatin in cultured human umbilical vein endothelial cells using DNA microarrays. Statins affected the expression levels of genes involved in inflammation, coagulation, and vascular constriction. The mRNA levels for interleukin-8 (IL-8) and monocyte chemoattractant protein-1 (MCP-1) decreased after statin treatment. Statins reduced mRNA levels of plasminogen activator inhibitor-1 (PAI-1) and increased the mRNA levels of thrombomodulin. Statins reduced the mRNA levels of endothelin-1 and increased the mRNA levels of nitric oxide synthase-3 (eNOS). These results show that, statins are clin. effective because of their ability to change the gene expression profile of endothelial cells thereby preventing vascular events.

IT 147511-69-1, Pitavastatin  
 RL: DMA (Drug mechanism of action); BIOL (Biological study)  
 (effect of statins on mRNA levels of genes related to inflammation, coagulation, and vascular constriction in HUVEC)  
 RN 147511-69-1 CAPLUS  
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:1007596 CAPLUS  
 DOCUMENT NUMBER: 140:65183  
 TITLE: Oil-containing, orally administrable pharmaceutical composition for improved delivery of a therapeutic agent  
 INVENTOR(S): Chen, Feng-Jing; Patel, Mahesh V.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Pat. Appl. 2002 32,171.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 13  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030235595	A1	20031225	US 2003-397969	20030325
US 6267985	B1	20010731	US 1999-345615	19990630 <--
US 6309663	B1	20011030	US 1999-375636	19990817 <--

US 20010024658	A1	20010927	US 2000-751968	20001229 <--
US 6458383	B2	20021001		
US 20020032171	A1	20020314	US 2001-877541	20010608 <--
US 6761903	B2	20040713		
WO 2004087052	A2	20041014	WO 2004-US9120	20040325
WO 2004087052	A3	20041118		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-345615	A2 19990630
US 1999-375636	A2 19990817
US 2000-751968	A2 20001229
US 2001-877541	A2 20010608
WO 2000-US18807	A 20000710
US 2003-397969	A 20030325

AB The present invention relates to oral pharmaceutical compns. and methods for improved delivery of therapeutic agents, e.g., lipid-regulating agents. Compns. of the present invention include a carrier, where the carrier contains a combination of a triglyceride and at least two surfactants, at least one of which is hydrophilic. Upon dilution with an aqueous

medium, the composition forms a clear, aqueous dispersion. The invention also

pertains to methods for treating lipid disorders such as hypercholesterolemia, hypertriglyceridemia, and mixed dyslipidemia by oral administration of the compns. provided.

IT 147511-69-1, Pitavastatin

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

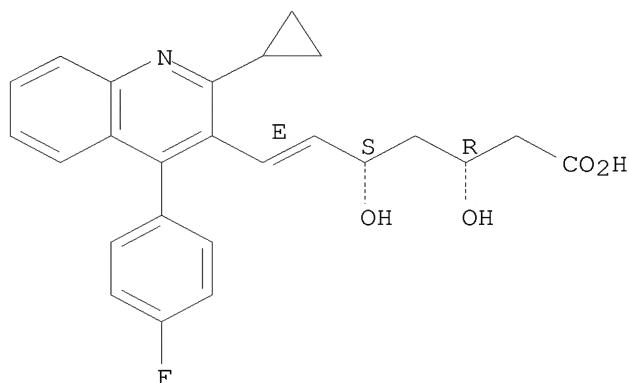
(oral composition containing triglyceride and surfactants for improved delivery of hydrophobic drugs)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinoliny]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

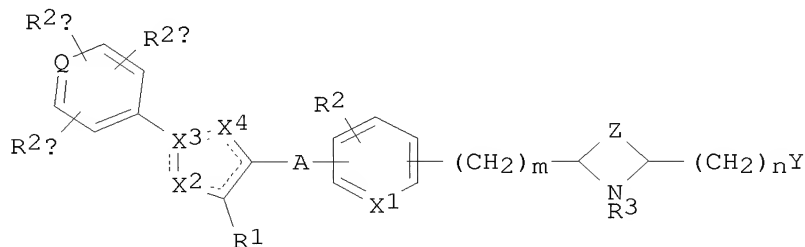
Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.

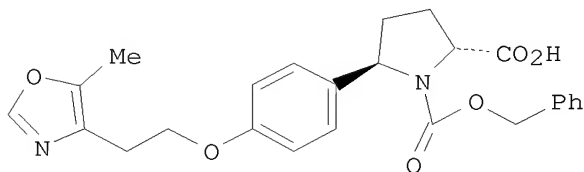


ACCESSION NUMBER: 2002:927184 CAPLUS  
 DOCUMENT NUMBER: 138:14048  
 TITLE: Preparation of oxazolylethoxyphenylprolines and related compounds as antidiabetic and antiobesity agents.  
 INVENTOR(S): Cheng, Peter T.; Jeon, Yoon; Wang, Wei  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096357	A2	20021205	WO 2002-US16628	20020523 <--
WO 2002096357	A3	20030925		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030092697	A1	20030515	US 2002-153342	20020522
US 7105556	B2	20060912		
CA 2449006	A1	20021205	CA 2002-2449006	20020523 <--
AU 2002310141	A1	20021209	AU 2002-310141	20020523 <--
EP 1401433	A2	20040331	EP 2002-737192	20020523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005506954	T	20050310	JP 2002-592870	20020523
HU 2006000226	A2	20061128	HU 2006-226	20020523
US 20060189598	A1	20060824	US 2006-406799	20060419
PRIORITY APPLN. INFO.:				
			US 2001-294505P	P 20010530
			US 2002-153342	A3 20020522
			WO 2002-US16628	W 20020523
OTHER SOURCE(S): MARPAT 138:14048				
GI				



I



II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH2)x, (CH2)x1, with an

alkenyl or alkynyl bond in the chain,  $(CH_2)_{x2}(CH_2)_{x3}$ ;  $x = 1-5$ ;  $x_1 = 2-5$ ;  $x_2, x_3 = 0-5$ ; provided that  $\geq 1$  of  $x_2$  and  $x_3 \neq 0$ ;  $X_1 = CH, N$ ;  $X_2 = C, N, O, S$ ;  $X_3 = C, N$ ;  $X_4 = C, N, O, S$  provided that  $\geq 1$  of  $X_2, X_3, X_4 = N$ ; in each of  $X_1-X_4$ , C may include CH;  $R_1 = H, alkyl$ ;  $R_2 = H, alkyl, alkoxy, halo, (substituted) amino$ ;  $R_2a, R_2b, R_2c = H, alkyl, alkoxy, halo, (substituted) amino$ ;  $R_3 = H, alkyl, arylalkyl, aryloxy, carbonyl, alkyloxy, carbonyl, alkynyloxy, carbonyl, alkenyloxy, carbonyl, aryl, carbonyl, alkyl, carbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroaryl, carbonyl, heteroaryl, heteroarylalkyl, alkyl, carbonyl, amino, aryl, carbonyl, amino, heteroaryl, carbonyl, amino, alkoxy, carbonyl, amino, aryloxy, carbonyl, amino, heteroaryl, carbonyl, amino, heteroaryl, heteroaryl, carbonyl, alkyl, sulfonyl, alkenyl, sulfonyl, heteroaryl, alkyloxy, carbonyl, cycloheteroalkyloxy, carbonyl, aryloxy, heteroaryl, alkyl, heteroaryl, alkyloxy, aryl, alkyl, aryl, alkyl, aryl, alkyl, aryl, alkyl, aryl, amino, aryl, alkyl, etc.$ ;  $Y = CO_2R_4, 1-tetrazolyl, P(O)(OR_4a)R_5, P(O)(OR_4a)_2$ ;  $R_4 = H, alkyl, prodrug\ ester$ ;  $R_4a = H, prodrug\ ester$ ;  $R_5 = alkyl, aryl$ ;  $Z = (CH_2)_{x4}, (CH_2)_{x5}, (CH_2)_{x6}O(CH_2)_{x7}$ ;  $x_4 = 1-5$ ;  $x_5 = 2-5$ ;  $x_6, x_7 = 0-4$ , were prepared as antidiabetic and antiobesity agents (no data). Thus, the title compound (II) was prepared in 6 steps.

IT 147511-69-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministration; preparation of oxazolylethoxyphenylprolines and

related

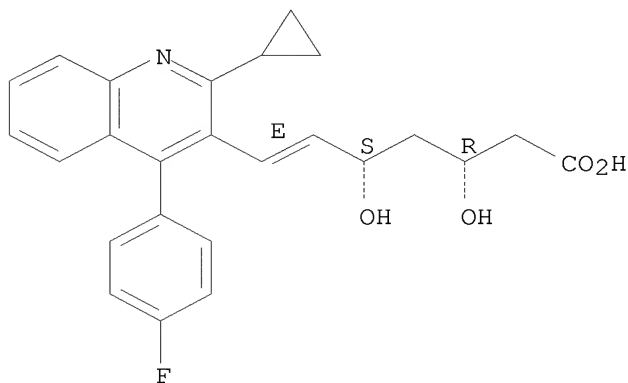
compds. as antidiabetic and antiobesity agents)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



L8 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:540258 CAPLUS

DOCUMENT NUMBER: 137:109267

TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors

INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 875,155.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020094977	A1	20020718	US 2001-7407	20011204 <--
US 6627636	B2	20030930		

US 20020013334 A1 20020131 US 2001-875155 20010606 <--  
 PRIORITY APPLN. INFO.: US 2000-211595P P 20000615  
 OTHER SOURCE(S): MARPAT 137:109267 US 2001-875155 A2 20010606  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

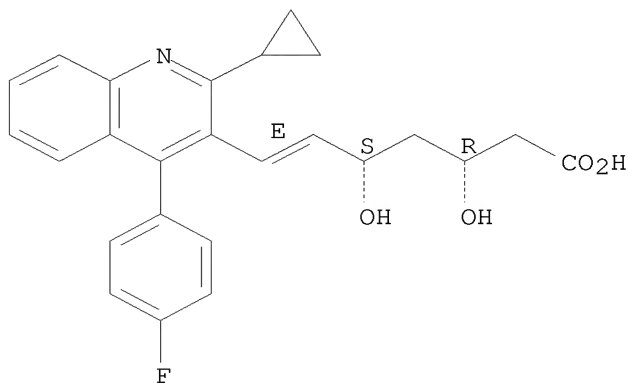
AB Title compds. I [X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>; Z = HOCHCH<sub>2</sub>CH(OH)CH<sub>2</sub>CO<sub>2</sub>R<sub>3</sub>, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R<sub>1</sub>, R<sub>2</sub> = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R<sub>3</sub> = H, alkyl, metal ion; R<sub>4</sub> = H, halo, CF<sub>3</sub>, etc.; R<sub>7</sub> = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R<sub>9</sub>, R<sub>10</sub> = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and atherosclerosis (no data). A multistep synthesis of II is reported.

IT 147511-69-1, Pitavastatin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.



L8 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2004:392331 CAPLUS  
 DOCUMENT NUMBER: 140:406798  
 TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors  
 INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 875,155, abandoned.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040092573	A1	20040513	US 2003-602752	20030624
US 6812345	B2	20041102		
US 20020013334	A1	20020131	US 2001-875155	20010606 <--
PRIORITY APPLN. INFO.:			US 2000-211595P	P 20000615
			US 2001-875155	B2 20010606

OTHER SOURCE(S): MARPAT 140:406798  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

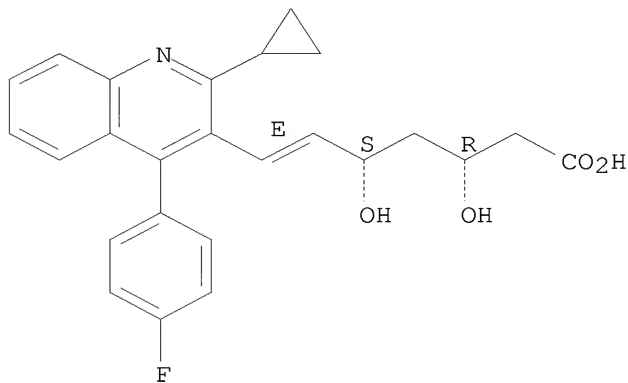
AB Title compds. I [X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>; Z = HOCHCH<sub>2</sub>CH(OH)CH<sub>2</sub>CO<sub>2</sub>R<sub>3</sub>, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R<sub>1</sub>, R<sub>2</sub> = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R<sub>3</sub> = H, alkyl, metal ion; R<sub>4</sub> = H, halo, CF<sub>3</sub>, etc.; R<sub>7</sub> = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R<sub>9</sub>, R<sub>10</sub> = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.

IT 147511-69-1, Pitavastatin  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
Double bond geometry as shown.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2002:777648 CAPLUS  
DOCUMENT NUMBER: 137:257659  
TITLE: Therapeutic combinations for cardiovascular and inflammatory indications  
INVENTOR(S): Seibert, Karen; Keller, Bradley T.; Isakson, Peter C.  
PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078625	A2	20021010	WO 2002-US9185	20020327 <--
WO 2002078625	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002306868	A1	20021015	AU 2002-306868	20020327 <--
US 20030199482	A1	20031023	US 2002-107809	20020328
CN 1527709	A	20040908	CN 2002-810210	20020328
PRIORITY APPLN. INFO.:				
			US 2001-279239P	P 20010328
			WO 2002-US9185	W 20020327

AB The invention provides therapeutic combinations and methods for treating or preventing a hypercholesterolemia-related or an inflammation-related condition in a subject in need of such treatment or prevention. One therapeutic combination comprises an Apical Sodium codependent Bile acid Transport (ASBT) inhibitor combined with COX-2 inhibitor. A further therapeutic combination comprises an ASBT inhibitor, a COX-2 inhibitor and an HMG Co-A reductase inhibitor. Another therapeutic combination comprises a chromene COX-2 inhibitor and an HMG Co-A reductase inhibitor.

IT 147511-69-1, Itavastatin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (HMG CoA reductase, cyclooxygenase and sodium codependent bile acid transport inhibitors for cardiovascular and inflammatory diseases in humans)

RN 147511-69-1 CAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).  
 Double bond geometry as shown.

